

9 Endocrine

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قال تعالى:

وَمَا مُحَمَّدٌ إِلَّا رَسُولٌ
 قَدْ خَلَتْ مِنْ قَبْلِهِ الرُّسُلُ

أَفَنْ مَاتَ أَوْ قُتِلَ نُفْقِلْتُمْ عَلَىٰ أَعْقَابِكُمْ
 وَمَنْ يَنْقَلِبْ عَلَىٰ عَقْبَيْهِ
 فَلَنْ يَضُرَّ اللَّهَ شَيْئًا
 وَيَجْزِي اللَّهُ الشَّاكِرِينَ

أل عمران ١٤٤

1. Diabetes Mellitus (DM) D4T

Def: Defined as (using venous sample):

Fasting blood glucose level

Or **random plasma glucose level** > 11.1 mmol/L (200 mg/dl)

See examination at the end of this chapter

N.B: in asymptomatic patients the measurements should be duplicated on another day before the diagnosis is made

لازم نفيس مرة ثانية في يوم تاني عشان نأكد التشخيص

Types of DM:

	Type I	Type II
Age	Usually young age < 40 years	Older patient > 50 years
Duration of symptoms	Weeks	Months to years
Body weight	Normal or low	Obese
Cause	Autoimmune β -cell destruction	Insulin resistance, β -cell dysfunction
Presentation	Polyuria, polydipsia, weight loss, keto-acidosis	Often asymptomatic presents with micro or macro vascular complications
Ketonuria	Yes	No
Rapid death without treatment with insulin	Yes	No
Treatment	Treated by diet and Insulin	Treated by oral hypoglycemics, Insulin, diet, life style modification

Common presentations

- Pain, numbness, paraesthesia, visual acuity changes, lassitude
- Recurrent skin infections

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Other causes of DM:

- Steroids, thiazides, Cushing's disease, pancreatitis

Diagnosis of DM:

By:

- Symptoms of hyperglycemia
- Increased venous glucose on 2 separate occasions
- Fasting ≥ 126 mg/dl
- Random ≥ 200 mg/dl
- Glucose tolerance test ≥ 11.1 mmol/L (200 mg/dl)

How to do 2hr glucose tolerance test

- Smoking cessation for 3 days
- الامتناع عن التدخين 3 أيام قبل التحليل
- Normal CHO diet for 3 days
- الصوم ليلة التحليل
- Give 75 gm glucose in 300 ml water to drink in the morning
- Measure blood glucose before the test and after 2 hours
- To convert from mmol/l to mg/dl multiply by 18
- Example: $11.1 \text{ mmol/l} \times 18 = 200 \text{ mg/dl}$

Symptoms of hyperglycemia

- Polyuria
- Polydipsia
- Unexplained wt loss
- Visual blurring
- Genital thrush
- Lethargy

Treatment of DM

Tip: Tablets & Insulin should not be used before an adequate trial of diet alone (2-3ml) unless the patient is very ill or has a very high blood glucose ($>25 \text{ mmol/l}$) $\geq 450 \text{ mg/dl}$

Life Style

- Regular exercise
- Diet
- ↓ Saturated Fats, ↓ Sugar
- ↑ Starch, CHO, Moderate Protein
- Stop smoking, foot care

2/5 خضروات 2/5 فاكهة 2/5 سبج 2/5 خبز 2/5 مكرونة 2/5 لبن 2/5 زيت 2/5 صلصة 2/5 مالحات

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Medication

- Type I is treated by Insulin
- Type II is treated by diet and exercise, oral anti-diabetic, Insulin

Oral hypoglycemics

- Generally: Start with metformin if (BMI) >25
- If BMI <25 use Metformin + sulfonylureas
- Insulin may be needed if this does not work

Biguanides (Metformin)

- Avoid if creatinine $>150 \text{ Umol/L}$ d.t. lactic acidosis
- Stop if tissue hypoxia (e.g. MI, sepsis)
- Stop before GA

Other Medications

- Acarbose: add on drug e.g. 50mg, chewed at start of each meal
- Meglitinides

Insulin

Members

Human insulins

1. Short acting

- Insulin lispro (analogue)
- Insulin aspart (analogue)
- Soluble insulin (clear)

Fast acting "can be taken immediately before food"

"Taken 30 min. before food"

2. Intermediate acting

- Isophan insulin "NPH" (cloudy) commonly mixed with soluble insulin

3. Long acting

- Insulin glargine "Lantus"

Uses

- Essential ttt for type I DM
- Treatment of some patients with type II DM

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Insulin regimen

- Design the insulin regimen to suit patients life style (diet, exercise) not vice versa
- The average **daily requirement is 0.5 unit/kg**
- Begin at least a total daily dose of 1 unit of insulin for every unit of BMI in adults

1. Twice daily biphasic insulin regimen: (the commonly used)

- Given twice daily (at the morning and at the evening)
- Contains (soluble + intermediate)
- Ex: Mexitard 30 (30 % soluble + 70 % Isophan)
- Patient will need to eat snacks, mid morning and during the evening
 - R: Give $\frac{2}{3}$ of the daily dose in the morning and $\frac{1}{3}$ in the evening
 - Ex: 70 kg man requires 36 units /d
give 24 units in the morning
give 12 unit in the evening

2. Basal bolus regimen

- Regular insulin before each meal + NPH (or Lantus) at bed time
- It is the best regimen in type 1 & uncontrolled type 2

Prescribing information

Type	Onset	Peak	Duration	Example
soluble insulin راق	0.5-1 hr	1-4	4-8 hr	Actrapid, Humalin R
Insulin aspart or lispro	< 0.5 hr	0.5-2.5	3-4.5 hr	Humalog, Novorapid
Isophan إسوفان	1-3 hr	3-8	7-14	insuman basal, insulatard

Insulin glargine	1-2	6-12	12-30	Lantus
Biphasic (Isophan/soluble)	Compound profile		Compound profile	Given once daily at bedtime in type 1 or II
				Mexitard 10,20,30

► All are given s.c except regular insulin (all routes)

Adverse effects

- The commonest side effect is hypoglycemia
- Patients taking insulin for a long time or who are taking β Bs may not develop classical symptoms
- β Bs don't block sweating which can be the only sign of hypoglycemia (see hypoglycemia topic)
- Lipodystrophy around injection sited SO rotate injection sites
- Other SE:** weight gain and peripheral oedema

Drug interactions:

- Insulin and sulfonylurea should not be combined with other antidiabetics.
- Effect of insulin is decreased by the action of corticosteroids and thiazides
- During pregnancy don't use antidiabetic drugs but use insulin

Safety and efficacy

- Patients should measure their own blood glucose 4 times daily
- Use ACEIs to protect the renal function whether the patient has HTN or HF or not.

Patient advice

- Continue taking insulin during acute illness (requirement increase)
- Drinking fluids is more important than eating
- Eat low saturated fat, low sugar, high starch, high CHO, moderate protein, stop smoking

Biguanides

- Metformin:** ↑ Insulin sensitivity

Uses:

- Treatment of type II DM
- Not a ttt for type I DM

Precautions:

- Don't give to patient with renal impairment (Cr. > 150 mmol/L)
- Avoid in severe hepatic insufficiency
- Avoid in pregnancy
- Pregnant diabetic woman should be treated with insulin**
- Metformin cause lactic acidosis, this can be fatal

Advice:

- Metformin does not cause weight gain → useful in obese
- If bl.g is ↑, metformin can be used with other drugs (combination)

Adverse Effects:

- Lactic acidosis, ↑ with renal impairment
- Gastrointestinal: nausea, vomiting, diarrhea & constipation
- To reduce this:** give it in divided doses with gradual increase 500mg for 1 week, 500mg b.i.d (twice daily), 500mg t.d.s. Can cause unpleasant metallic taste

Drug Interactions

- Avoid NSAIDs or any drug that can worsen reduced renal function.
- Monitor renal function; withdraw the drug if there is significant impairment.
- Cardiovascular assessment is important, also assess lipid profile.

Prescribing Information

- Initially start with 500 mg. PO with breakfast for at least 1 week
- ↑ the dose to 500 mg. 3 times daily
- The usual **maximum dose is 2gr.** In divided doses, can be ↑ to 3g/d in rare cases

In the Market

R/Metformin tabs (500mg.)
R/Cidophage (500mg.)
R/Cidophage retard (850mg.)
R/Glucofage (500, 1000mg.)

Sulfonylureas (↑ Insulin production)

Members:

Gliclazide
Glipizide
Gliquidone
Tolbutamide
Glimepride (long acting)
Glibenclamide (long acting)

Uses:

- Treatment if DM Type II
- Not a Treatment if DM Type I

Take Care:

- Don't give them to patients é severe hepatic insufficiency
- Avoid in pregnancy
- Avoid in severe hypersensitivity to sulfonamides
- Long acting drugs as glibenclamide can cause hypoglycemia greater than short acting
- Take care in renal impairment & elderly patients
- Self usually cause weight gain

- Drug Interactions**
1. Effect of Sulfonylurea is usually reduced by the action of Corticosteroids and thiazides
 2. Metabolism is inhibited by anti-fungal drugs (itraconazole & fluconazole)
 3. Avoid combination as they ↑ risk of hypoglycemia

Prescribing Information (all sulfonylurea are equal in effect)

1. Gliclazide

- Initially 40 - 80 mg. é breakfast PO
- Maximum daily dose is 320 mg.
- Doses above 100mg. should be divided

Gliclazide is short acting → must be given twice daily except MR which is given once daily before breakfast

Trade Names

R/Diamicon MR (30, 60)
R/Diamicon

2. Glibenclamide: Long acting

- Initially 5mg. with breakfast PO
- Maximum daily dose is 15mg./d
- Reduce the initial dose to 2.5 mg. in the elderly → cause 2 peaks of hypoglycemia.

Trade Names

R/Glibenase (5mg.)
R/Daonil (5mg.)

3. Glimepiride:

R/Amaryl (1mg, 2mg, 3mg, 4mg) 1x1
R/Dolcyl (1mg, 2mg, 3mg) 1x1
R/Diabonor (2mg, mg) 1x1

4. Metformin + Glibenclamide

R/Glucovance 500+2, 500+2.5 1x1

Other antidiabetics

1. Meglitinides

A. Nateglinide

PO, initially 60mg. 3x/day (with meals)
Max. dose = 180 3x/day

- R/Starlix 120mg (Nateglinide)

R/Starlix combine (Nateglinide + Metformin 500mg)

B. Repaglinide

- PO, initially 500 µg 3x/day (with meals)
- Max. dose 24mg. 3x/day
- R/Novonorm (0.5, 1, 2mg)
- R/Diaryl (0.5, 1, 2mg)

2. Glitazones (insulin sensitizers)

A. Pioglitazone

- By mouth 15-45mg/day
- R/Actozone (30, 45mg)
- R/Glustin (15, 30mg)

B. Rosiglitazone

- PO, initially 4mg/day
- May ↑ to 8mg/day (single or divided doses) after 8 weeks treatment if required.
- R/Avandia 4mg

Diabetic Foot care

1. عند غسل القدمين يجب تخفيفها جيدا خاصة بين الأصابع ، كما يجب مراعاة اختبار حرارة الماء قبل استخدامه كي لا يسبب حرقا للجلد .
2. يتم فحص القدمين يوميا وخاصة القدمية ، الجانبين ، الكعب وبين الأصابع واستشارة الطبيب (طبيب القدم أو جراح الأوعية الدموية) عند ظهور أية تقرحات أو علامات للتلف .
3. يجب ارتداء حذاء وجوارب وخاصة في الطقس البارد تجنباً لحدوث لسعة البرد على أن يكون جوارب نظيفة ويجب رطاب الحذاء الجوارب التي تضغط على الساقين و المزودة برباط من الصوف .
4. يتم وضع كريم مرطب على القدمين بعد غسلها إذ أن جلد مريض السكري يكون جافا وقد يشقق مما قد يؤدي إلى الإصابة بالالتهابات .
5. كما ينبغي المحافظة على القدمين بارتداء الحذاء المناسب والمرح أيضا ويجب فحص الحذاء من الداخل باستمرار تقريبا لوجود أي شيء بداخله قد يؤدي القدمين والتهاب بخلع الحذاء بعد ساعات من ارتدائه لتغير نقاط الضغط على القدمين .
6. عدم المشي طويلا حافيتين أبدا تجنباً لأي إصابات محتملة .
7. يتم فحص القدمين بالماء البارد قبل قص الأظافر وقصها مستقيمة غير ملفنة

• See Atlas 9 p273, 274

2. Hypothyroidism D₄R

- Common and easy to treat

Symptoms:

- Tiredness & lethargy
- Depression
- Dislike of cold
- Weight gain
- Constipation
- Menorrhagia
- Hoarse voice
- Poor cognition, dementia
- Myalgia

Signs:

- Dry skin & hair
- Non-pitting oedema (eyelids, hands & feet)
- Bradycardia
- Peripheral neuropathy
- There may be goiter

Diagnosis

- Serum TSH & free T₄
- If TSH is high, measure free T₄, if it is low hypothyroidism is confirmed.

Management

1. Refer those who are young or ill

2. Treatment:

- Oral levothyroxine (T₄) → R/Eltroxin (50,100)
- If healthy or young start with 50-100µg/day PO, review at 12 weeks, and adjust every 6 weeks to normalize TSH but not suppress it.
- If old (elderly) or cardiac: start with 25µg/day & 1 dose by 25µg every 4 weeks according to TSH (but cautiously as thyroxine may precipitate angina or MI)
- Check TSH every month and stop increasing thyroxine when TSH is normal
- The usual maintenance dose of thyroxine is 100-200µg/day & is lifelong.

- N.B if the TSH is suppressed in young people the thyroxine dose should be lowered to avoid osteoporosis.

Follow up:

- Once stable, TSH should be monitored annually.

References:
1. OHCM: p204, 205
2. GP: p111, 112

3. Hyperthyroidism and Thyrotoxicosis D₄R

Symptoms

- Weight loss despite increase appetite
- Heat intolerance
- Sweating
- Diarrhea/hyperdefecation
- Tremors

Signs:

- Tachycardia (may be AF)
- Warm peripheries
- Fine tremors
- Palmar erythema
- Hair thinning
- Lid lag (eyelid lags behind eye's descent as patient watches your finger descend slowly)

Irritability/nervousness

- Emotional lability & psychosis
- Itching
- Oligomenorrhea: may cause infertility

- Lid retraction (exposure of sclera above iris causing "staring look")

- In Graves' disease only: Exophthalmos, periorbital myxoedema, oedematous swelling above the lateral malleoli, thyroid acropathy (See thyroid examination later)

Diagnosis:

- TSH ↓, T₄ and T₃ ↑

Treatment (by specialist)

- Refer all patients to endocrinology. The aetiology must be determined.

1. Use propranolol 40mg/6hrs for rapid relief of symptoms

R/Inderal tab (10, 40)

2. Start carbimazole 20-40 mg/day

R/Carbimazole 5mg Neo-Mercazole 5mg

- And maintaining the dose until the patient is euthyroid usually after 4-8 weeks.

- The commonest causes are:
o Graves' disease (80% of cases)
o Toxic multinodular goiter
o Toxic adenoma.

- Then reduce the dose progressively to a maintenance of 5-15 mg/day.
- Assess every 6 months with TFTs
- Carbimazole is usually continued for 12-18 months
- On stopping, check TFTs, follow-up beyond 1 year is not necessary.

3. Radioactive iodine

References:
1. OHCMP 202, 203
2. GP 112, 113

4. Examination of the patient with diabetes

In general you should be alert to:

1. CVS complications
2. Renal dse.
3. Retinal dse.
4. Peripheral Neuropathy
5. Health of insulin injection sites
6. The diabetic foot.

Important points for diabetic examination:

A. Inspection: Look for:

- Hydration
- Weight
- Hyperpigmentation

B. Legs:

- Ms wasting
- Hair loss
- Skin atrophy
- Skin pigmentation
- Leg ulceration (especially around pressure points & toes)
- Skin infections

C. Associated skin lesions

• Necrobiosis Lipoidica diabetorum:

Plaque like reddened area with central area that fades to white-yellow found on anterior surface of the legs: in these areas the skin becomes very thin & can ulcerate easily

D. Injection sites:

- Inspect and palpate for fat atrophy, fat hypertrophy or local infection.

E. Neurological Examination:

- Visual acuity
- Fundoscopy (by expert)
- Peripheral sensory neuropathy: evidence of injury, ulceration, test MS strength & examine feet.

F. Full cardiovascular examination.

Frame work for diabetic foot examination

Inspection:

- Colour
- Ulceration
- Dryness
- Callous Formation
- Infection
- Evidence of injury: shoes rubbing?
- Charcot's joints (grossly abnormal & dysfunctional joints due to repeated minor trauma & poor healing d.t loss of pain sensation)

Key points for diabetic foot examination

1. Neuropathy (clinically)
2. Ischemic (clinically + Doppler + angiogram)
3. Bone deformity e.g. Charcot's joint (clinically + x-ray)
4. Infection (swab, blood culture, x-ray)

Neurology:

- 10 g monofilament test (استخدام خيط بلاستيكي بمسح خفيف 10g)
- Light touch sensation
- Pain sensation
- Vibration sense
- Joint position sense (proprioception)

Circulation:

- Peripheral pulses (dorsalis pedis & posterior tibial)
- Temperature
- Capillary filling time

Remember complications of DM

Microvascular neuropathic

1. Retinopathy: cataract, impaired vision.
2. Nephropathy: protein loss, renal failure.
3. Peripheral neuropathy: sensory loss, motor weakness.
4. Autonomic neuropathy: postural hypotension, vomiting, diarrhea.
5. Foot disease: ulceration, arthropathy.

Macrovascular

1. MI/ ischemia
2. Claudication, gangrene, amputation.
3. Transient ischemic attack (TIA), stroke.

References:
1. Oxford handbook of clinical examination & practical skills p120, 121

5. Examination of the thyroid gland

- The patient should be sitting upright on a chair of the edge of a bed

Inspection

- Enlarged (goiter) or not? - You may notice it protruding as a swelling just below the thyroid cartilage.
- Normal thyroid gland is usually **neither visible nor palpable**.
- Thyroid gland lies 2-3 cm below the thyroid cartilage & has 2 equal lobes connected by a narrow isthmus
- If you noticed swelling - ask the patient to **take a mouthful of water then swallow** and watch the neck swelling carefully. Also ask the patient to **protrude their tongue** & watch:
 1. The thyroid is attached to the thyroid cartilage and will move with swallowing
 2. Other neck masses such as enlarged LNs will **hardly move**
 3. Thyroglossal cysts will **not move** with swallowing but will move up with protrusion of the tongue.

Palpation

- Always begin palpation **from behind**
- Stand behind the patient & place a hand either side of their neck
قف خلف المريض وضع يديك على جانبي رقبته
- The patient's neck should be slightly flexed to relax the sternomastoid.

Explain what you are doing

- Ask if there is any tenderness
- Place the middle 3 fingers of either hand along the midline of the neck just below the chin
- Gently "walk your fingers down" until you reach the thyroid gland
- the central isthmus is almost never palpable
- If enlarged: symmetrical or not?
- Are there any discrete nodules?
- Assess the size, shape & mobility of any swelling
- Repeat the examination whilst the patient swallows



Consistency:

1. **Soft:** Normal
2. **Firm:** Simple goiter
3. **Rubbery hard:** Hashimoto's thyroiditis
4. **Stony hard:** cancer, cystic calcification, fibrosis.

- Feel the **palpable thrill** which may be present in metabolically active thyrotoxicosis.

► In retrosternal enlargement the percussion note over the manubrosternum is dull as opposed to the normal resonance.

6. Assessing thyroid status

1. Observe the patient: relaxed, agitated?
2. Measure the HR & note for atrial fibrillation
3. Inspect the hands:
 - Erythema
 - Warmth
 - Thyroid acropathy (phalangeal bone overgrowth)

Remember complications of DM

Microvascular neuropathic

1. **Retinopathy:** cataract, impaired vision.
2. **Nephropathy:** protein loss, renal failure.
3. **Peripheral neuropathy:** sensory loss, motor weakness.
4. **Autonomic neuropathy:** postural hypotension, vomiting, diarrhea.
5. **Foot disease:** ulceration, arthropathy.

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3. Inspect the hands:
 - Erythema
 - Warmth
 - Thyroid acropathy (phalangeal bone overgrowth)

4. Look for peripheral tremors
 - Ask the patient to stretch out their arms with fingers out straight & palms down.
 - Resting a piece of paper on the back of the hand can make a tremor more obvious

5. Inspect the face

- Exophthalmos, proptosis
- Hypothyroid features

6. Examine the eyes

7. Examine the thyroid

8. Look for peritibial myxoedema

References:
1. Oxford handbook of clinical examination & practical skills p 116, 117

Put in your mind

1. In examining diabetic patient be alert to hydration, ms wasting, weight loss, leg ulceration, insulin injection sites, peripheral neuropathy, visual acuity, any CVS problem, any renal problem.
2. Thyroid swelling:
 - **Soft:** normal
 - **Firm:** simple goiter
 - **Rubbery hard:** Hashimoto's thyroiditis
 - **Stony hard:** cancer, cystic calcification, fibrosis
3. In retrosternal enlargement of thyroid: percussion over manubriosternum is dull as opposed to the normal resonance.
4. Thyroid acropathy = phalangeal bone overgrowth
5. C/P of hypothyroidism may be: tiredness, weight gain, hoarse voice, dislike of cold, constipation, dry skin, hair, peripheral neuropathy, non pitting oedema, may be goiter.
6. C/P of Hyperthyroidism may be: Heat intolerance, weight loss, sweating, diarrhea, tremors, psychosis, irritability, itching, tachycardia, hair thinning, eye signs (lid lag, lid retraction, peritibial myxoedema).

Test yourself

1. Mestard is composed of
2. Mention the types of the following:
 - Actrapid
 - Novorapid
 - Mestard
 - Lantus
 - Insulatard
 - Humalin R
3. Drugs causing DM
4. Main complications of DM are
5. Headlines of tt of DM are
6. Causes of DM II are
7. Causes of DM I are
8. Lid lag is a sign of
9. DM is defined as
10. Mention the active ingredient for the following:
 - Cedophage
 - Diamicon
 - Glabonase
 - Amaryl
 - Glucovance
 - Eltroxin
 - Inderal
11. During pregnancy, major operation we use instead of in tt of DM
12. Regarding oral antidiabetic drugs:
 - If BMI is < 25 we use
 - If BMI is > 25 we use
13. All types of insulin are give i.c except
14. Symptoms of hyperglycemia are
15. Mestard is administered as following:

Answers

1. 30 % Soluble insulin, 70 % isophan
2. Soluble
 - Insulin aspart or lispro
 - Biphasic
 - Glargin
 - Isophan
 - Soluble
3. Steroid, thiazides
4. Retinopathy, nephropathy, peripheral neuropathy
5. Life style modification, insulin, oral hypoglycemic
6. Insulin resistance, β cell dysfunction
7. Autoimmune destruction of β cells
8. hyperthyroidism
9. fasting bl glucose > 200mg/dl
10. Metformin
- Glucalade

- Glibenclamide
- Glimperide
- Combined
- T4
- Propionolol
- 11. Insulin, oral drugs
- 12. Metformin + sulfonylurea
- Mediamin
- 13. Regular insulin (all routes)
- 14. Polyuria
- Polydipsia
- Unexplained wt loss
- Visual blurring
- Genital thrush
- Lethargy
- 15. % in the morning, % in the evening

فصل ال Endocrine والله تعالى الفضل والمنة